AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning on page 5, line 3 with the following paragraph:

Also described in the Japanese Patent Kokai Publication is an amorphous substance of 8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one or a salt thereof, which possesses an action to inhibit ~~acetylcholine esterase~~acetylcholinesterase.

Please replace the paragraph beginning on page 7, line 26 with the following paragraph:

There has also been a desire in the pharmaceutical industry to attain crystals that are good in absorbability and are used ~~for~~ as an ~~acetylcholine esterase~~acetylcholinesterase inhibitor, an agent for improving the excretory potency of a urinary bladder, and a therapeutic agent against micturition disorders/dysuria disorders which are stable.

Please replace the paragraph beginning on page 10, line 16 with the following paragraph:

(12) Agent for improving excretory potency of the urinary bladder which comprises a combination of an α-blocker and an amine compound of non-carbamate-type having an ~~acetylcholin esterase~~acetylcholinesterase-inhibiting action; and

Please replace the paragraph beginning on page 10, line 22 with the following paragraph:

(13) Crystals of a tricyclic, condensed, heterocyclic derivative and pharmaceutical compositions comprising the crystals, which possess an action to inhibit ~~acetylcholine esterase~~acetylcholinesterase and an action to improve the excretory potency of urinary bladder.

Please replace the paragraph beginning on page 10, line 29 with the following paragraph:

In other words, the present invention also relates to

(i) crystals of 8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one or a salt thereof,

(ii) the crystals described in the above-mentioned item (i), wherein the melting point is above 110°C,

(iii) the crystals described in the above-mentioned item (i), wherein the melting point is about 113°C to about 118°C,

(iv) a pharmaceutical composition which comprises the crystals described in the above-mentioned item (i),

(v) the pharmaceutical composition described in the above-mentioned item (iv), which is an ~~acetylcholine esterase~~acetylcholinesterase inhibitor,

(vi) the pharmaceutical composition described in the above-mentioned item (iv), which is an agent for improving the excretory potency of urinary bladder,

(vii) the pharmaceutical composition described in the above-mentioned item (iv), which is a therapeutic agent against micturition disorders,

(viii) the pharmaceutical composition described in the above-mentioned item (iv), which is a therapeutic agent against dysuria disorders, and

(ix) agents for improving the excretory potency of urinary bladder, which are characterized by combining crystals of 8-[3-[1-[(3-fluorophenyl)methyl]-4-piperidinyl]-1-oxopropyl]-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-ij]quinolin-4-one or a salt thereof with an α-blocker.

Please replace the paragraph beginning on page 95, line 8 with the following paragraph:

The crystals of the present invention have an activity to inhibit ~~acetylcholine esterase~~acetylcholinesterase. Therefore, the crystals of the present invention and the pharmaceutical compositions of the present invention can be used as the prophylactic and/or therapeutic agents against the senile dementia.

Please replace the paragraph beginning on page 95, line 19 with the following paragraph:

Also, the crystals of the present invention and the pharmaceutical compositions of the present invention can be used, for example, as agents for improving the excretory potency of urinary bladder. For instance, they can be used as the prophylactic and/or therapeutic agents against micturition disorders arising from the following 1) to 6) and the like, dysuria in particular: 1) ~~Prostatic~~ prostatic hypertrophy, 2) bladder neck obstruction, 3) neurogenic bladder, 4) diabetes mellitus, 5) surgery, 6) hypotonic bladder, and 7) Sjoegren's syndrome (dry eye, dry mouth, dryness of vagina, and the like).

Please replace the paragraph beginning on page 96, line 11 with the following paragraph:

The crystals of the present invention are those of a kind of non-carbamate amine compound possessing the action to inhibit ~~acetylcholine esterase~~acetylcholinesterase. A non-carbamate amine compound including that for the crystals of the present invention, which possesses the action to inhibit acetylcholinesterase~~acetylcholine esterase~~, can be used in combination with a drug to treat diseases inducing micturition disorders (for example, dysuria and the like) or with a drug that is administered to treat other diseases but as itself induces micturition disorders (for example, dysuria and the like).

Please replace the paragraph beginning on page 96, line 31 with the following paragraph:

Such a "non-carbamate amine compound possessing the action to inhibit acetylcholinesterase~~acetylcholine esterase~~" may be any compound possessing the action to inhibit acetylcholinesterase~~acetylcholine esterase~~ and not having the carbamate structure (-OCON-) within the molecule, wherein the hydrogen atom of ammonia is substituted with a hydrocarbon group, preferably being the primary amine compound, the secondary amine compound, or the tertiary amine compound. More preferably, there are set forth compounds 1) to 49) and the like that are described in the following. Among these compounds, compounds, which have at least one 5- to 7-membered, nitrogen-containing heterocyclic ring as a partial structure, and the like are preferable; compounds 1), 20), 23), 41), and 43), which are described hereinafter, and the like

are especially preferable~~,~~ ; and compound 1) and the like are particularly preferable.

Hereupon, because a variety of non-carbamate amine compounds described above possess the action to inhibit the acetylcholinesterase~~acetylcholine esterase~~, they possess also an insecticidal action.

Please replace the paragraph beginning on page 125, line 7, with the following paragraph:

The following Examples are drawn to the embodiments of the present invention involving crystals. The melting points were measured by using a Type-535 melting point apparatus produced by Büchi~~Buechi~~ Company and a MP-500D apparatus manufactured by Yanako Kiki Kaihatsu Kenkyusyo Kabushiki Kaisya. The data on the powder X-ray crystal diffractometry are determined by using Type-RINT1100 (Rigaku Denki Kabushiki Kaisya) using the Cu-Kα_1 radiation as the radiation source. Also, in the following Reference Examples and Examples, % indicates the percent by weight, unless otherwise specified.

Please replace the paragraph at page 129, line 7 to line 16 with the following paragraph:

Data of X-ray powder diffraction analysis

Diffraction angle: 2θ(°)~~2θ (°)~~	Spacing: Spacing: d value~~d value~~ (angstrom)
5.08	17.4
10.2	8.68
16.8	5.27
17.8	4.97
18.6	4.76
20.6	4.31
23.1	3.85

Please <u>delete</u> the paragraphs beginning on page 130, line 2 through line 31.

~~According to a procedure similar to that used in Formulation Example 4, there were prepared 2,000 tablets of 3 mm in diameter, each of which contains 1.0 mg of the crystals obtained in Example 1.~~

~~Formulation Example 6~~

~~(1)Crystals in Example 1 5.0 mg~~

~~(2)Lactose 60.0 mg~~

~~(3)Corn Starch 35.0 mg~~

~~(4)Gelatin 3.0 mg~~

~~(5)Magnesium 2.0 mg~~

~~By the use of 0.03 ml of 10% aqueous solution of gelatin (containing 3.0 mg of gelatin), a mixture of the above-described substances (1), (2), and (3) was granulated by passing through a sieve with a 1-mm mesh and the resulting granules were dried at 40°C and then sieved again. The thus-obtained granules were mixed with the above-described (5) and pressed. The thus-obtained core tablets were sugar-coated by treatment with a suspension of sucrose, titanium dioxide, talc, and gum arabic in water. The resulting sugar-coated tablets were glazed with wax to obtain the coated tablets.~~

~~Experimental Example 5~~

~~Determination of the activity to inhibit the acetylcholine esterase~~

~~The activity to inhibit the acetylcholine esterase of the crystals obtained in Example 1 was determined according to the acetylthiocholine method (the Ellman method) by the use of a human erythrocyte-derived acetylcholine esterase.~~

~~A human erythrocyte-derived acetylcholine esterase (Sigma Chemical Company) was dissolved into distilled water to obtain a standard enzyme preparation with an enzyme concentration of 0.2 IU/mL. To a 96-well titer plate were dispensed 20 μl of the drug-containing solution, 30 μl of an 80-mM solution of Tris-HCl (pH 7.4), 50 μl of the standard enzyme preparation, and 50 μl of a 5-mM solution of 5,5-dithio-bis(2-nitrobenzoic acid) (Sigma Chemical Company) and the microplate was shaken for 10 seconds. As soon as 50 μl of a 4-mM solution of acetylthiocholine iodide (Sigma Chemical Company) was added and shaking was started again, every increment in~~

Please replace the paragraph beginning on page 131, line 19 with the following paragraph:

Determination of the activity to inhibit the ~~acetylcholine esterase~~acetylcholinesterase

Please replace the paragraph beginning on page 131, line 20 with the following paragraph:

The activity to inhibit the acetylcholinesterase~~acetylcholine esterase~~ of the crystals obtained in Example 1 was determined according to the acetylthiocholine method (the Ellman method) by the use of a human erythrocyte-derived acetylcholinesterase~~acetylcholine esterase~~.

Please replace the paragraph beginning on page 131, line 23 with the following paragraph:

A human erythrocyte-derived acetylcholinesterase ~~acetylcholine esterase~~ (Sigma Chemical Company) was dissolved into distilled water to obtain a standard enzyme preparation with an enzyme concentration of 0.2 IU/mL. To a 96-well titer plate were dispensed 20 μl of the drug-containing solution, 30 μl of an 80-mM solution of Tris-HCl (pH 7.4), 50 μl of the standard enzyme preparation, and 50 μl of a 5-mM solution of 5,5-dithio-bis(2-nitrobenzoic acid) (Sigma Chemical Company) and the microplate was shaken for 10 seconds. As soon as 50 μl of a 4-mM solution of acetylthiocholine iodide (Sigma Chemical Company) was added and shaking was started again, every increment in absorbance at the wavelength of 414 nm at an interval of 30 seconds was determined for 10 minutes.

$$R = 5.74 \times 10^{-7} \times \Delta_A$$

(wherein R indicates an enzyme activity (mol) and Δ_A indicates an increment in absorbance at the wavelength of 414 nM). The experiment was repeated at least three times with each compound to determine the 50% inhibitory concentration (IC_{50}). Furthermore, the activity to inhibit the acetylcholinesterase~~acetylcholine esterase~~ of distigmine was determined in a manner similar to that described in the above method. The results obtained are shown in the following Table.

Compounds	IC_{50} (nM)
Example 1	6.6

Distigmine 651.9

Please replace the paragraph beginning on page 132, line with the following paragraph:

The results described above reveal that the crystals of the present invention possess an excellent activity to inhibit the acetylcholinesterase~~acetylcholine esterase~~.

Please replace the paragraph beginning on page 134, line 5, with the following paragraph:

The crystals of the present invention possess an excellent action to inhibit acetylcholinesterase~~acetylcholine esterase~~ and an action to improve the excretory potency of urinary bladder and are low in the toxicity, thereby being useful as drugs. Also, the crystals of the present invention are high in ~~the~~ purity, high in ~~the~~ quality, low in ~~the~~ their hygroscopic property, and extremely excellent in ~~the~~ their stability without being deteriorated upon a long-term storage under the usual conditions.